

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> C07K 1/00, 14/00, 17/00, A21C 3/06, 3/08, B28B 11/08, 21/48, 21/98, B29C 53/00, 53/14, C12N 5/00, 5/02	<b>A1</b>	<b>(11) International Publication Number:</b> WO 00/50445 <b>(43) International Publication Date:</b> 31 August 2000 (31.08.00)
<b>(21) International Application Number:</b> PCT/US00/04838 <b>(22) International Filing Date:</b> 25 February 2000 (25.02.00) <b>(30) Priority Data:</b> 60/121,787 26 February 1999 (26.02.99) US <b>(71) Applicant (for all designated States except US):</b> OKLAHOMA MEDICAL RESEARCH FOUNDATION [US/US]; 825 N.E. 13th Street, Oklahoma City, OK 73104 (US). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> CONAWAY, Joan, A. [US/US]; 10801 East Apple Valley Road, Oklahoma City, OK 73151 (US). CONAWAY, Ronald, C. [US/US]; 10801 East Apple Valley Road, Oklahoma City, OK 73151 (US). KAMURA, Takumi [JP/US]; 7016 Chestmount Drive, Ok- lahoma City, OK 73132 (US). <b>(74) Agent:</b> GUFFEY, Wendell, Ray; Mead Johnson & Company, 2400 West Lloyd Expressway, Evansville, IN 47721 (US).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> NOVEL COMPONENT OF VON HIPPEL-LINDAU TUMOR SUPPRESSOR COMPLEX AND SCF UBIQUITIN LIGASE		
<b>(57) Abstract</b> <p>Rbx1, an evolutionarily conserved Cullin-interacting RING-H2 finger protein, has been discovered. Mammalian Rbx1 has been identified as a component of the CUL2-containing VHL complex. An Rbx1 homolog from <i>S. cerevisiae</i> has also been identified as a subunit and activator of the Cdc53-containing SCF<sup>Cdc4</sup> ubiquitin ligase required for ubiquitination of the cdk inhibitor Sic1 and for the G1/S cell cycle transition in yeast, providing a link between the multiprotein VHL tumor suppressor complex and cellular ubiquitination. The Rbx1 protein acts as a cellular marker useful (1) in detecting a possible predisposition to certain carcinomas, (2) as a molecular target for treating those carcinomas therapeutically, (3) as a target for inhibition by drugs that manipulate the growth of cells, and (4) as a research tool to better understand the various complex mechanisms of cell ubiquitination, binding of certain activator proteins, fibronectin deposition and other aspects of the cellular division process.</p>		